06-1405

AF

TRANSMITTAL OF APPEAL BRIEF

Docket No.
HO-P02086US1

In re Application of: James R. Lupski et al.

Application No.	Filing Date	Examiner	Group Art Unit
10/021,955	December 13, 2001	S. Chunduru	1637

Invention: DEFECTS IN PERIAXIN ASSOCIATED WITH MYELINOPATHIES

TO THE COMMISSIONER OF PATENTS:

Transmitted herewith is the Appeal Brief in this application, with respect to the Notice of Appeal filed: April 12, 2005 .

The fee for filing this Appeal Brief is $ 500.00 .

[x] Large Entity [ ] Small Entity

[ ] A petition for extension of time is also enclosed.

The fee for the extension of time is _____ .

[x] A check in the amount of $ 500.00 is enclosed.

[ ] Charge the amount of the fee to Deposit Account No. _____ .
This sheet is submitted in duplicate.

[ ] Payment by credit card. Form PTO-2038 is attached.

[x] The Director is hereby authorized to charge any additional fees that may be required or credit any overpayment to Deposit Account No. 06-2375 .
This sheet is submitted in duplicate.

Melissa L. Sistrunk

Dated: June 13, 2005

Melissa L. Sistrunk
Attorney Reg. No. : 45,579
FULBRIGHT & JAWORSKI L.L.P.
Fulbright Tower
1301 McKinney, Suite 5100
Houston, Texas 77010-3095
(713) 651-3735

Appeal Brief Transmittal

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as Express Mail, Airbill No. EV 670374607US, in an envelope addressed to: MS Appeal Brief - Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date shown below.

Dated: June 13, 2005 Signature: Monica L. Thomas (Monica L. Thomas)

PTO/SB/17 (12-04v2)
Approved for use through 7/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Effective on 12/08/2004.
Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).

FEE TRANSMITTAL
For FY 2005

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 500.00

Complete if Known	
Application Number	10/021,955
Filing Date	December 13, 2001
First Named Inventor	James R. Lupski
Examiner Name	S. Chunduru
Art Unit	1637
Attorney Docket No.	HO-P02086US1

METHOD OF PAYMENT (check all that apply)

☒ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): _____

☐ Deposit Account Deposit Account Number: 06-2375 Deposit Account Name: Fulbright & Jaworski L.L.P.

For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

☐ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, **except for the filing fee**

☒ Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17 ☒ Credit any overpayments

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

	FILING FEES		SEARCH FEES		EXAMINATION FEES		
Application Type	**Fee ($)**	**Small Entity Fee ($)**	**Fee ($)**	**Small Entity Fee ($)**	**Fee ($)**	**Small Entity Fee ($)**	**Fees Paid ($)**
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description	**Fee ($)**	**Small Entity Fee ($)**
Each claim over 20 (including Reissues)	50	25
Each independent claim over 3 (including Reissues)	200	100
Multiple dependent claims	360	180

Total Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
_____	- 20 =	_____	x _____	=	_____

Multiple Dependent Claims

Fee ($)	**Fee Paid ($)**
_____	_____

Indep. Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
_____	- 3 =	_____	x _____	=	_____

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		**Extra Sheets**		**Number of each additional 50 or fraction thereof**	**Fee ($)**	**Fee Paid ($)**
_____	- 100 =	_____	/50	_____ (round **up** to a whole number)	x _____	= _____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English Specification, $130 fee (no small entity discount)	
Other (e.g., late filing surcharge): 1402 Filing a brief in support of an appeal	500.00

SUBMITTED BY

Signature	Melissa L. Sistrunk	Registration No. (Attorney/Agent)	45,579	Telephone	(713) 651-3735
Name (Print/Type)	Melissa L. Sistrunk			Date	June 13, 2005

Fee Transmittal

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as Express Mail, Airbill No. EV 670374607US, in an envelope addressed to: MS Appeal Brief - Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date shown below.

Dated: June 13, 2005 Signature: Monica L. Thomas (Monica L. Thomas)

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as Express Mail, Airbill No. EV670374607US , in an envelope addressed to: Commissioner for Patents, Alexandria, VA 22313-1450, on the date below:

Date: June 13, 2005

Monica L. Thomas

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Lupski *et al.*

Application Serial No.: 10/021,955

Filed: December 13, 2001

For: Baylor College of Medicine

Group Art Unit: 1637

Examiner: Chunduru, S.

Atty. Dkt. No.: P02086US1

Title: Defects in Periaxin Associated with Myelinopathies

APPEAL BRIEF

Commissioner for Patents
Washington, D.C. 20231

Melissa L. Sistrunk
Agent for Applicant
Registration No.: 45,579
FULBRIGHT & JAWORSKI L.L.P.
1301 McKinney, Suite 5100
Houston, Texas 77010-3095
(713) 651-3735
(713) 651-5246 (Fax)
msistrunk@fulbright.com

TABLE OF CONTENTS

Page

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as Express Mail, Airbill No. EV 670374607US , in an envelope addressed to: Commissioner for Patents, Alexandria, VA 22313-1450 on the date below:

Date: June 13, 2005

Monica L. Thomas

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Lupski *et al.*

Application Serial No.: 10/021,955

Filed: December 13, 2001

For: Baylor College of Medicine

Group Art Unit: 1637

Examiner: Chunduru, S.

Atty. Dkt. No.: P02086US1

Title: Defects in Periaxin Associated with Myelinopathies

APPEAL BRIEF

MS Appeal Brief
Commissioner of Patents
Washington, D.C. 20231

Sir:

Appellant hereby submits an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences in response to the final Office Action dated January 12, 2005 (the "Action"). The Notice of Appeal was filed on April 12, 2005.

The fee for filing this Appeal Brief is $500.00 and is enclosed herewith. Please date stamp and return the attached postcard as evidence of receipt.

06/15/2005 MAHMED1 00000053 10021955
01 FC:1402 500.00 OP

I. REAL PARTY IN INTEREST

The real parties in interest are the assignee, Baylor College of Medicine, and the licensee, Athena Diagnostics, Inc.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

III. STATUS OF THE CLAIMS

Claims 1-40 were originally filed. An Office Action setting forth restriction of the claims was mailed on February 19, 2003 and responded to on June 17, 2003, therein amending claims 2, 7, 35, 36, and 37, canceling claims 8-34, and adding claims 41-42.

An Office Action was mailed on July 23, 2003, and a Response to this Action was filed on December 18, 2003, in which claims 1 and 35 were amended; claim 41 was canceled, and claims 43-50 were added.

An Office Action was mailed April 30, 2004. A Response thereto was filed on August 25, 2004, therein amending claims 1, 4, 35, 40, and 43 and adding new claims 51-61.

A final Office Action was mailed January 12, 2005 rejecting claims 1-7, 35-40, and 42-61. Thus, claims 1-7, 35-40, and 42-61 are pending on appeal and are the subject of this appeal brief.

A copy of the pending claims is attached as Appendix 1.

IV. STATUS OF AMENDMENTS

There are no outstanding amendments in the pending claims.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

The present invention concerns diagnosing myelinopathy in an individual, wherein the myelinopathy results from a periaxin alteration, by obtaining a sample containing nucleic acid from said individual and assaying the sample for an alteration in a periaxin polynucleotide,

wherein the assaying step provides said diagnosis (in the specification at least at paragraphs **[0007]** and **[0047]**). In particular embodiments, specific periaxin polynucleotides are employed (in the specification at least at paragraph **[0064]**).

In particular embodiments, the myelinopathy is Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSN), congenital hypomyelinating neuropathy (CHN), or Roussy-Levy syndrome (RLS) (in the specification at least at paragraphs **[0007]** and **[0042]**). Assaying methods include polymerase chain reaction, for which specific primers are provided, in certain aspects of the invention (in the specification at least at paragraph **[0007]** and **[0046]**). Also, particular alterations in the periaxin polynucleotide are provided, such as alteration is 3775G>A, 1216G>A, 4075-4077d, 1483G>C, 3394A>G, 3248C>G, 2763A>G, 2645C>T, 306C>T, 1491C>G, 2655T>C, 2145T>A, 1102C>T, 2289delT, 2787delC, 2857C>T, or 247ΔC, for example (in the specification at least at paragraphs **[0009]**, **[0046]**, **[0048]**, and **[0061]**. In certain aspects of the invention, the alteration comprises a homozygous periaxin mutation or a compound heterozygous periaxin mutation (in the specification at least at paragraph **[0244]**).

In other embodiments of the invention, there are methods of detecting the presence or absence of a mutation associated with a myelinopathy that results from a periaxin mutation in the individual by isolating a test nucleic acid from a subject, wherein the test nucleic acid comprises a periaxin polynucleotide; comparing the test nucleic acid to a reference wild-type periaxin polynucleotide; and determining the differences between the test nucleic acid and the reference wild-type periaxin polynucleotide, wherein the differences are mutations in the periaxin polynucleotide of the subject, and wherein said detection of the presence or absence of the mutation is therein provided (in the specification at least at paragraph **[0021]**). Again, specific mutations and periaxin polynucleotides are provided, in specific embodiments (in the specification at least at paragraph **[0064]**). In additional specific embodiments, the mutation encodes a defect of a periaxin polypeptide, wherein the defect is R953X, R368X, S929fsX957, R196X, V763fsX774, C715X, or R82fsX96 (in the specification at least at paragraph **[0022]**). In other specific embodiments, the mutation encodes a defect of a periaxin polypeptide, wherein the defect is E1259K, A406T, E1359delΔ, E495Q, R1132G, P1083R, I921M, A882V, T102T, P497P, or P885P (in the specification at least at paragraph **[0022]**).

In additional embodiments of the invention, there are methods of diagnosing myelinopathy in an individual by obtaining a sample containing nucleic acid from the individual; and assaying the sample for an alteration in a periaxin polynucleotide, wherein the alteration is associated with the myelinopathy, and wherein the myelinopathy comprises a prominent sensory neuropathy, wherein the assay provides the diagnosis (in the specification at least at paragraphs **[0007]** and **[0273]**). In certain aspects of the invention, the alteration comprises a homozygous periaxin mutation or a compound heterozygous periaxin mutation.

In other embodiments, there are also methods of detecting a polymorphism or mutation in a periaxin polynucleotide of an individual, by obtaining a sample comprising the periaxin polynucleotide from the individual; and assaying the periaxin polynucleotide for the polymorphism or mutation (in the specification at least at paragraphs **[0007]** and **[0041]**). In specific aspects of the invention, the periaxin polynucleotide comprises SEQ ID NO:76 (in the specification at least at paragraph **[0064]**) and the myelinopathy is Dejerine-Sottas syndrome (in the specification at least at paragraph **[0007]**). In further specific embodiments, the individual is suspected of having the myelinopathy (in the specification at least at paragraph **[0244]**).

In additional aspects of the invention, there are methods of identifying an individual suspected of having myelinopathy or being a carrier of myelinopathy, by obtaining from said individual a sample comprising nucleic acid; and assaying the sample for an alteration in a periaxin polynucleotide, wherein the presence of the alteration identifies the individual as having periaxin-associated myelinopathy or being a carrier of periaxin-associated myelinopathy (in the specification at least at paragraphs **[0022]** and **[0244]**). In specific embodiments, the myelinopathy comprises a prominent sensory neuropathy (in the specification at least at paragraph **[0273]**). In further specific embodiments, the alteration comprises a homozygous periaxin mutation (in the specification at least at paragraph **[0244]**). In additional specific embodiments, the alteration comprises a compound heterozygous periaxin mutation (in the specification at least at paragraph **[0244]**).

In another embodiment of the invention, there is a method of identifying an individual suspected of having myelinopathy or being a carrier of myelinopathy, by obtaining from the individual a sample comprising genomic DNA having two PRX alleles; and assaying the sample for an alteration in a periaxin polynucleotide, wherein the presence of the alteration in the periaxin polynucleotide is indicative of an alteration in at least one of the PRX alleles, wherein

the presence of the alteration in both PRX alleles identifies the individual as having periaxin-associated myelinopathy and wherein the presence of the alteration in one allele identifies the individual as being a carrier of periaxin-associated myelinopathy (in the specification at least at paragraphs **[0244]-[0246]** and **[0273]**).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 1-7, 35-40, and 42-61 are rejected under 35 U.S.C. §112, first paragraph as allegedly failing to meet the enablement requirement.

VII. ARGUMENT

A. Substantial Evidence Required to Uphold the Examiner's Position

As an initial matter, Appellant notes that findings of fact and conclusions of law by the U.S. Patent and Trademark Office must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706(A), (E), 1994. *Dickinson v. Zurko*, 527 U.S. 150, 158 (1999). Moreover, the Federal Circuit has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by "substantial evidence" within the record. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000). In *Gartside*, the Federal Circuit stated that "the 'substantial evidence' standard asks whether a reasonable fact finder could have arrived at the agency's decision." *Id.* at 1312.

Accordingly, it necessarily follows that an Examiner's position on Appeal must be supported by "substantial evidence" within the record in order to be upheld by the Board of Patent Appeals and Interferences.

B. The Specification Enables a Skilled Artisan to Make and Use the Invention

Claims 1-7, 35-40, and 42-61 are rejected under 35 U.S.C. 112, first paragraph, because the Examiner alleges that the specification does not enable one of skill in the art to make and use the invention commensurate in scope with the claims. Appellants respectfully disagree with the Examiner.

1. The Courts have Interpreted the Standard for Enablement under 35 U.S.C. 112, first paragraph

The general standard for enablement under §112, first paragraph has been addressed in the case law repeatedly. For example, in *In re Wright*, 999 F.2d 1557, 27 U.S.P.Q.2d 1510 (Fed. Cir. 1993), the court stated that an enabling Specification teaches those skilled in the art how to make and use the claimed invention in its full scope without "undue experimentation." *Wright*, 999 F.2d at 1560. It is well-settled patent law that the first paragraph of § 112 requires nothing more than objective enablement. *In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971). This objective enablement may be provided through broad terminology or illustrative examples. *Id.* The PTO bears the initial burden, in rejecting a claim under the enablement requirement of §112, to set forth "a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the Specification of the application." *Wright*, 999 F.2d at 1561-62 (citing *Marzocchi*, 439 F.2d at 223-24, 169 U.S.P.Q. at 369-70).

Moreover, it is not necessary that a patent applicant test all the embodiments of his invention. *Amgen Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1213, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991) (citing *In re Angstadt*, 537 F.2d 498, 502, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976)). Section 112 requires simply that the patent applicant provide a disclosure which sufficiently enables one skilled in the art to carry out the invention commensurate with the scope of the claims. *Amgen*, 927 F.2d at 1213.

As has been determined by the courts, the scope of the enablement must only bear a "reasonable correlation" to the scope of the claims. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Even if experiments are necessary, a considerable amount of routine experimentation is permissible, especially where the Appellants' specification provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed. *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976).

In fact, time-consuming experiments are acceptable if the type of experimentation is standard in the art. An extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance. *In re Colianni,* 561 F.2d 220, 224, 195 USPQ

150, 153 (CCPA 1977). Yet further, the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Wands*, 858 F.2d 737, 8 USPQ2d 1404 (Fed. Cir. 1985); *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom. Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine" *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)).

Examples may be either "working" or "prophetic", and compliance with the requirements for enablement under 35 U.S.C. 112 does not require that an example is disclosed, or that the invention be reduced to practice prior to filing, *Gould* v. *Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987) and M.P.E.P. 2164.02, and it is well-settled case law that a specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

Furthermore, the Federal Circuit has held that § 112 does not require that the applicant describe exactly the subject matter claimed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991). Moreover, it is not necessary that a patent applicant test all the embodiments of his invention. *Amgen Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1213, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991) (citing *In re Angstadt*, 537 F.2d 498, 502, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976)). Section 112 requires simply that the patent applicant provide a disclosure which sufficiently enables one skilled in the art to carry out the invention commensurate with the scope of the claims. *Amgen*, 927 F.2d at 1213.

In discussing claim breadth, M.P.E.P. § 2164.03 provides that:

> The scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required.

M.P.E.P. § 2164.03, 2100-116 (1995). Should the Examiner feel that the present invention is directed to an art where certain results may be associated with a degree of unpredictability, M.P.E.P. § 2164.03 also supports Appellants' position on enablement rather than that advanced in the Action. M.P.E.P. § 2164.03 further provides:

> It is well settled that in cases involving chemicals and chemical

> compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result.

Id. (quoting *In re Dreshfield*, 45 U.S.P.Q. 36 (C.C.P.A. 1940)).

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970), and guidance is not necessary to those skilled in the art, particularly when it is well-recognized that the skill in the art of molecular biology is quite high (*Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986)

Moreover, it is unnecessary to teach all potential embodiments, as disclosure of well-known techniques or scientific principles to those of skill in the art is not required. *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBC v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 U.S.P.Q. 481, 489 (Fed. Cir. 1984).

Appellants remind the Board that the present invention is directed to an art where certain results may be associated with a degree of unpredictability, but M.P.E.P. § 2164.03 also supports Appellants' position on enablement rather than that advanced in the Action. M.P.E.P. § 2164.03 further provides:

> It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result.

Id. (quoting *In re Dreshfield*, 45 U.S.P.Q. 36 (C.C.P.A. 1940)).

Even if the claims encompass inoperative embodiments, such as where alterations are not associated with a myelinopathy, this is not prohibited by the statutes. The Federal Circuit has explained that the fact that claims may encompass inoperative embodiments does not necessarily render them non-enabled, or invalid. *Atlas Powder Co. v. E. I. duPont de Nemours & Co.*, 224

U.S.P.Q. 409, 414 (Fed. Cir. 1984). It is not the function of the claims to exclude possible inoperative substances. *Atlas Powder*, 224 U.S.P.Q. at 414.

Section 112 simply requires that there be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill in the relevant art how to make and use the invention as broadly as it is claimed (emphasis added). *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Satisfaction of the enablement requirement is not precluded by the necessity of some experimentation. *Atlas Powder Co. v. E.I. DuPont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984). In *Angstadt*, the predecessor court to the Federal Circuit found that disclosure of many operable embodiments and one inoperative embodiment did not render a claim broader than the enabled scope because determination of the operable embodiments did not involve undue experimentation. *In re Angstadt*, 537 F.2d 498, 502-503, 190 USPQ 214, 218 (CCPA 1976).

Determination of whether a rejection is appropriate based on the scope of a claim relative to the scope of the enablement depends on two factors: 1) how broad the claim is with respect to the disclosure; and 2) if one skilled in the art is enabled to make and use the entire scope of the invention without undue experimentation. M.P.E.P. §§ 2164.08. Appellants assert that the claims are not too broad, given the amply disclosure and guidance therein, and that undue experimentation is not required by the skilled artisan to make and use the invention.

2. Appellants' Specification is Enabling for the Scope of the Claims

The instant specification is commensurate with the scope of the pending claims, directed generally to methods of diagnosing myelinopathies by identifying an alteration in a periaxin polynucleotide sequence. Appellants have provided multiple exemplary embodiments of periaxin alterations that are associated with a myelinopathy, such as the specific mutations noted at least in paragraph **[0061]** and the exemplary myelinopathies identified at least in **[0042]**, and have also provided teachings concerning how to identify additional mutations wherein the periaxin alteration associates with a periaxin mutation. For example, at paragraphs **[0244]** to **[0246]**, **[0249]**-**[0250]**, and **[0264]**-**[0282]**, Appellants provide exemplary methods for identifying mutations in a sequence and associating those mutations with an exemplary myelinopathy, DSN.

In particular, Appellants assert that there are a considerable number and content of working examples commensurate with the scope of the claims. For example, in Example 1 (paragraphs **[0235]** to **[0241]**), Appellants provide materials and methods to practice exemplary

embodiments of the invention, including obtaining the periaxin polynucleotide, mapping it, and screening for mutations, such as by PCR. Example 2 (paragraphs **[0242]-[0243]**) provides characterization of the *PRX* gene, including a tissue expression profile, *in situ* hybridization by FISH, and sequencing. Example 3 (paragraphs **[0244]-[0246]**) provides teaching of *PRX* mutation analysis in 168 peripheral neuropathy patients who had tested negative for mutations in *PMP22, MPZ, GJB1, EGR2*, or *MTMR2*. Even though alterations in *PRX* are described for unaffected family members, it is well-known in the field how to correlate a particular mutation with a disease, as stated in Dr. Lupski's affidavit.

Furthermore, Example 8 shows that *PRX* mutations are related to a spectrum of demyelinating neuropathies (in paragraph **[0268]**): "These two families confirm that putative loss-of-function mutations in *PRX* cause autosomal recessive neuropathies and ***broaden the spectrum of PRX-associated peripheral neuropathies***." (emphasis added) Also (in paragraph **[0273]**): "Similar to the spectrum of phenotypes observed with mutation of other genes associated with CMT and related inherited peripheral neuropathies, the clinical phenotypes manifested in patients with mutations in *PRX* include CMT myelinopathies and DSN." As such, Appellants note that the invention has been utilized to evaluate thousands of neuropathy patients during the last few years (Athena Diagnostics, Inc.).

Appellants assert that there are more than sufficient number and content of working examples provided in the specification to support association of *PRX* mutations with a range of myelinopathies within the CMT1 category. Appellants teach in paragraphs **[0062]** and **[0268]** that mutations in periaxin cause human peripheral myelinopathies, given that multiple unrelated DSN patients with recessive *PRX* mutations were identified, as well as families associated with the spectrum of *PRX*-associated peripheral neuropathies. Appellants also provide a variety of means to obtain sequence information (paragraph **[0063]**) and a voluminous number of exemplary periaxin polynucleotide sequences (paragraph **[0064]**) to assay for mutations in an analysis.

Importantly, the specification in paragraphs **[0074]** through **[0083]** discuss different exemplary embodiments of myelinopathies having similar and overlapping phenotypes directed to at least defects in myelin, but also onion bulb defects (found in CMT1, DSN, and CHN); slowed motor nerve condution velocities (NCV) (found in CMT1, HNPP, DSN, and CHN); muscle weakness (CMT1 and CHN); gait disturbance or ataxia (CMT1 and RLS); and areflexia

(CHN and RLS), for example. This is clear evidence that this is a ***group of highly-related diseases having significant phenotypic overlap*** likely to associate with *PRX* defects. Appellants are not trying to claim periaxin for a wide range of diseases but those as part of a phenotypically narrow range of myelinopathies. The specification states in paragraph **[0263]**: "The association of mutations in *PRX* with peripheral neuropathy not only identifies another genetic cause for the *CMT1 spectrum of myelinopathies* but also provides further insights into the molecular mechanisms *for these diseases*." (emphasis added) This was even set forth in post-filing references, at least such as the peer reviewed journal article of Takashima *et al.* (2002) (related to the instant specification).

Finally, although Appellants' instant specification was enabling, Appellants bring the attention of the Board to multiple papers published since the filing of the application teaching periaxin alterations that are associated with myelinopathies other than DSN. In fact, patients from four unrelated demyelinating neuropathy families, three manifesting DSN and one with a severe demyelinating CMT, CMT4F, have recessive *PRX* nonsense and frameshift mutations (Boerkoel *et al.*, 2001 (related to the instant specification); Guilbot *et al.*, 2001; Delague *et al.*, 2000). For example, Guilbot *et al.* (2001) teach that periaxin is responsible for an autosomal recessive form of CMT disease. Also, Kijima *et al.* (2004) determined that periaxin mutation causes early onset CMT. Given that Appellants taught in the original disclosure that alterations in periaxin are indicative of myelinopathies, these subsequent papers indicate that Appellants in fact did provide how to make and use the invention, and the claims are thus enabled.

3. The Examiner is Applying an Incorrect Standard for Enablement

Appellants assert that the Examiner incorrectly rejected the pending claims for enablement by applying an improper standard thereto, particularly given the interpretation of the standard for enablement based on multiple court cases and given the ample teachings in the enabled specification, as detailed above.

The crux of the Examiner's arguments, elaborated at least on Pages 4, 7, 8, 14, and 20 of the Action, concerns allegations that the specification has not established a predictable correlation for an association between any periaxin mutation and any myelinopathy or specific myelinopathy. Furthermore, on at least Pages 7 and 8, the Examiner notes that the art is silent with regard to a predictable association between any specific alteration or mutation in periaxin

and a representative number of diseases encompassed by the term "myelinopathy." Appellants favorably acknowledge the Examiner's assessment of the art.

Appellants assert that a predictable correlation is not required for enablement of the present invention. In the specification, Appellants have provided multiple exemplary embodiments of periaxin alterations that are associated with a myelinopathy and have also provided teachings concerning how to identify additional mutations wherein the periaxin alteration associates with a periaxin mutation (for example, at paragraphs **[0244]** to **[0246]**, **[0249]-[0250]**, and **[0264]-[0282]**, at the very least in addition to the routine knowledge of the skilled artisan. This is sufficient to satisfy the standards of enablement.

Nevertheless, Appellants fully address the Examiner's rejection and address the allegation that a predictable correlation is necessary between a periaxin mutation and a myelinopathy. The predictable correlation is in fact that the defect in a periaxin polynucleotide is associated with a myelinopathy, ***as the claims state***, and myelinopathies are each units of a spectrum of closely-related diseases. That is, it is predictable that there are periaxin mutations that are diagnostic of a myelinopathy, based on Appellants' teachings, yet it is not necessary for Appellants to describe each and every one; it is certainly unnecessary to provide more than the representative number of mutations described therein, given that the methods to identify additional ones are provided.

On Page 4 of the Action, the Examiner contends that there is no statistically significant association between all of the mutations disclosed therein and any myelinopathy. The Examiner considered Appellants' arguments in at least the previous Response filed August 25, 2004, which stated that only a reasonable correlation is required for enablement. Although the Appellants did indeed provide at least an exemplary periaxin mutation with DSN as correlative to the highly related myelinopathies and methods how to determine others, the Examiner considered this non-persuasive. Appellants reiterate that it is not required to provide statistically significant data for enablement of a claim; this is simply not the standard required by the USPTO. As has been determined by the courts, the scope of the enablement must only bear a "reasonable correlation" to the scope of the claims. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Appellants assert that a reasonable correlation has been provided by showing periaxin mutation with the exemplary myelinopathy DSN; also, there is a reasonable correlation with the highly-related myelinopathies, particularly given their art-recognized phenotypic similarities (such as

those described in paragraphs **[0074]** to **[0083]**. Furthermore, given that others subsequently identified periaxin mutations in myelinopathies within the spectrum of myelinopathies that include DSN, commensurate with Appellants' teaching, there is most certainly a reasonable correlation between periaxin mutations and myelinopathies in general, particularly when the claims require that the myelinopathy is a result of a periaxin alteration. Thus, the Examiner is inappropriately requiring statistically significant data for enablement of a claim.

The Examiner further states that the specification has not established that "any periaxin mutation is associated with DSN" (Page 4 of the Action). Appellants assert that it is not a requirement to list each and every periaxin mutation that results in myelinopathy, given that a representative number of mutations have been provided, in addition to methods of how to obtain others.

On Pages 4, 9, and 19 of the Action, the Examiner contends that the specification fails to establish that the presence of a single mutation in a single allele would indicate that someone is susceptible to myelinopathy or a carrier of a periaxin-associated myelinopathy, since there are mutations in periaxin that are "not only not diagnostic but also not associated with myelinopathy (Table 2)." The Examiner further notes on Pages 5 and 12 of the Action that there are examples in the specification wherein the presence of the mutation is not associated with the disease, and further states on the bridging sentence between Pages 5 and 6 that unaffected control subjects contain mutations in periaxin. The Examiner concludes on Page 6 that the mere detection of an alteration in periaxin is not diagnostic for myelinopathies in general and extrapolates that there allegedly is no guidance as to which periaxin alterations are disease-associated.

Appellants reiterate that the specification teaches the following at the ending of paragraph **[0244]**:

> The unaffected parents and son of family HOU579 are each ***heterozygous carriers of a PRX mutant allele*** (FIG. 3). Families HOU418, HOU579 and HOU297 exhibit autosomal recessive inheritance. Black symbols indicate DSN. Patient 851 from family HOU297 is compound heterozygous for mutations S929fsX957 and R953X; her older normal son is heterozygous for R953X. Patient 1461 from family HOU579 is compound heterozygous for mutations V763fsX774 and R368X; her normal brother is heterozygous for V763fsX774. Patient 1136 from family HOU418 has the homozygous mutation S929fsX957; her two normal sisters and her son are heterozygous for this mutation. (emphasis added)

The Examiner misconstrues this passage by saying that it teaches PRX mutations are not associated with myelinopathy. In fact, this passage teaches that individuals can be carriers for the mutation for the disease by being heterozygous for the mutation; this is absolutely classical genetics and does not indicate that PRX mutations are NOT associated with myelinopathies.

However, Appellants consider the Examiner's acknowledgement that carriers for the mutations exist, but that there allegedly has been no guidance as to identification of a carrier. Regarding Table 2 on page 67 of the application, for example, these sequence alterations merely represent benign polymorphic variants, which are common in human genetics. Upon being presented with a sequence alteration, a skilled artisan would know how to identify them as disease-causing of specific myelinopathies, given the level of skill in the art and presence of sufficient working examples in the disclosure and the art. This is even acknowledged by a skilled artisan in the declaration filed with the Response on December 18, 2003 by co-inventor and genetics expert Dr. James Lupski. As stated therein, one skilled in the art would be able to make and use the claimed invention employing the application as a guide, and the references published soon thereafter in the art reporting additional periaxin mutations in other myelinopathies is proof of this point. In particular, the affidavit states as follows:

> The Examiner also expresses concern about the unpredictability of identifying whether a sequence variation is a polymorphism or a disease-causing mutation, but in diseases such as those myelinopathies that comprise an autosomal recessive nature (see, at least, paragraphs **[0062]**, **[0242]**, **[0244]**, **[0246]**, **[0247]**, **[0260]**, **[0261]**, **[0268]**, and **[0273]**), it is significant that mutations on both alleles must be present before the disease occurs, whether as a homozygote or compound heterozygote. That is, it is highly unlikely with an affected family that two non-diseased parents of a diseased individual would be carriers of the same polymorphism. In fact, if the myelinopathy had an inheritance pattern other than autosomal recessive, we would be able to easily identify this, as well.
>
> ***Moreover, a skilled artisan recognizes how to discern between a polymorphism and a disease-causing mutation. If the sequence alteration is a polymorphism, it is not identified in controls and/or does not segregate with the disease phenotype. By definition in the field of human genetics a polymorphism has to be observed in 1% of chromosomes. Thus, the absence of such a variant in 50 control normal individuals (i.e. 100 control chromosomes) is inconsistent with the variant representing a polymorphism.*** (emphasis added)

Therefore, one of skill in the art would recognize a polymorphism *vs.* a disease-causing mutation based on routine practices utilized in the art. Appellants refer the Board to *In re Oelrich*, 579 F.2d 86, 198 USPQ 210 (CCPA 1978), which states that the opinions of experts are based on their competence bearing the level of ordinary skill in the art and are sufficient to shift the burden of going forward with the evidence back to the PTO. Furthermore, with this shift in the burden, the Examiner cannot dismiss a declaration without adequate explanation of ***why*** the declaration failed to overcome the rejections (*In re Alton*, 76 F.3d 1168, 1174 37 USPQ2d 1578, 1583 (Fed. Cir. 1996)), when in fact the affidavit specifically addressed this and other issues.

The Examiner also presumes that a large amount of experimentation would be required to practice the invention as claimed, given that allegedly there is no predictable correlation with any periaxin mutation and any myelinopathy (Pages 9 and 18 of the Action). The Examiner supposes that to practice the invention as claimed, one of skill in the art would have to perform a large study of patients with different types of myelinopathy, such as CMT, DSN, and matched controls, to determine if any general or specific alteration or mutation in periaxin was associated with any myelinopathy in general. The Examiner further takes for granted that such a study would consist of trial and error and that the outcome would be unpredictable and that it would require a large amount of experimentation to identify which mutations were associated with myelinopathy and which were not associated with myelinopathy (Pages 9 and 21 of the Action). Also, the Examiner contends that the specification does not provide guidance or direction as to which mutations would have a significant effect, nor does it allegedly provide guidance as to which direction the experimentation should proceed, other than to actually assess each alteration. Experimentation to "predict which mutations would fall within the scope of the claimed invention" is considered undue, and Appellants strongly disagree.

First, in addressing these allegations, Appellants note that multiple periaxin mutations for other myelinopathies were reported soon after filing, so obviously the experimentation was ***not*** undue, and if those of skill in the art cannot be held as a standard for what is undue, then the Examiner is clearly mistaken. Appellants reiterate that undue experimentation is not required to determine which nucleotide alterations are associated with myelinopathy. The Examiner contends that a large amount of trial and error would be required to determine which mutations are associated with the disease.

Given that both the co-inventor states in an affidavit that a skilled artisan recognizes methods to identify myelinopathy disease-causing periaxin alterations and given that others did in fact achieve this post-filing of the application, it is clear that even if it was trial and error, this was not undue and that a ***reasonable*** amount of routine experimentation ***was*** employed.

No undue experimentation is required to make and use the invention as claimed, particularly given that Appellants provide detailed characteristics of exemplary mutations associated with DSN and related myelinopathies (such as at least in Example 8). The identification of exemplary mutations associated within the spectrum of myelinopathies provides a disclosure that more than sufficiently enables the scope for myelinopathies, particularly given that the ability to associate mutations with particular diseases is achieved by well-known means in the art (such as is described in paragraphs **[0244]** to **[0246]**.

Furthermore, it is not unpredictable for a skilled artisan to be able to determine whether or not a particular sequence variation is associated with a disease state, and, in fact, it is routine to do so. Even within the CMT family itself, a variety of mutations in other genes have been associated with the disease (see paragraph **[0004]**), yet Appellants remind the Board that pending claims 1, 35, 43, and 57 and their dependent claims regard only those myelinopathies resulting from a periaxin alteration.

Appellants assert that they have provided ***both*** sufficient numbers of periaxin mutations (at least six exemplary mutations) and associating myelinopathies (at least five exemplary myelinopathies) and appropriate language enabling the invention to associate a particular mutation with a specific myelinopathy. The correlation between particular mutations and disease states is performed by well-known means in the art, and the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The postfiling reporting by others of additional periaxin mutations associated with myelinopathies other than the exemplary DSN myelinopathy of Appellants' specification shows that enough guidance was present in the application or within the routine level of the skill in the art, or both.

The Examiner focuses on Appellants' arguments that Appellants are not claiming a wide range of diseases but a "phenotypically narrow range of myelinopathies" (Page 11 of the Action), which is referred to by the skilled artisan inventors in the application as a spectrum of

myelinopathies associated with a periaxin mutation (at least at paragraphs **[0004]**, **[0080]**, **[0263]**, and Example 8). The point is that Appellants are not claiming identification of an alteration in a wide spectrum of any disease, such as the diverse continuum of cancer, for example, but in a directed range of myelinopathies. At the very least, claims 4 and 40 are certainly enabled, given that Appellants list very specific myelinopathies therein. Furthermore, at the very least claim 58 regards a prominent sensory neuropathy, which does not include a wide range of myelinopathies.

Appellants emphasize that the pending independent Claims 1, 35, 43, and new claim 57 require that the myelinopathy results from or is associated with a periaxin alteration. Therefore, these pending claims do not cover myelinopathies resulting from mutations in other polynucleotides, and the scope is not so broad as the Examiner contends. In addressing arguments from Appellants' previous Response that the claims are drawn not to any myelinopathy but to those associated with an alteration in periaxin, the Examiner contends on Page 12 of the Action that the specification has not provided a predictable way for the skilled artisan to determine if mutations are associated or which types of myelinopathies would be considered myelinopathy resulting from a periaxin alteration. Appellants reiterate that predictability is not required, and that trial and error in identifying the mutation(s) or any other means to do so is clearly achievable, given that Appellants have provided teachings in the specification regarding such and that others achieved the same end result postfiling of the application.

The Examiner reviewed the papers published since the application filing and considered them to be non-persuasive, because they did not provide a predictable correlation that all alterations in periaxin result in myelinopathies in general, any specific myelinopathy, or which periaxin mutations are associated with myelinopathy mutations (Page 13 of the Action). Appellants reiterate that a predictable correlation is not required, other than the prediction that a periaxin mutation will be diagnostic of a myelinopathy, which was demonstrated not only by Appellants but by others.

In the previous Response filed August 25, 2004, the Appellants asked the Examiner to reconsider the declaration filed by inventor and skilled artisan Dr. James Lupski concerning the specification's teachings that mutations in periaxin cause a broad spectrum of demyelinating neuropathies and how to recognize and assess a difference in a polymorphism and disease-

causing mutation. The Examiner addresses this point on Page 16 of the Action, by reiterating that specific mutations are not noted as predictive of or even associated with myelinopathy. However, the Examiner does not state why the declaration from the skilled artisan was so easily dismissed. Although the Examiner considers that the declaration addresses polymorphisms *vs.* disease-causing alterations, the Examiner reiterates that experimentation is required to determine whether an alteration was diagnostic or associated with myelinopathies. Appellants are unclear why the Examiner does not recognize that others in the art, who allegedly were not provided a predictable correlation by the Examiner's standards, still identified periaxin mutations in a variety of myelinopathies. This proves that either a predictable correlation was not necessary or that Appellants' teachings were sufficient to provide a predictable correlation. However, experimentation is not precluded, according to the courts, and the Examiner provides no ***evidence*** why the statements of the skilled artisan were not persuasive that polymorphisms *vs.* disease-causing mutations are easily discernible. To reiterate, the opinions of experts are based on their competence bearing the level of ordinary skill in the art and are sufficient to shift the burden of going forward with the ***evidence*** back to the PTO (*In re Oelrich*, 579 F.2d 86, 198 USPQ 210 (CCPA 1978)), and the Examiner cannot dismiss a declaration without adequate explanation of ***why*** the declaration failed to overcome the rejections (*In re Alton*, 76 F.3d 1168, 1174 37 USPQ2d 1578, 1583 (Fed. Cir. 1996)).

On Page 17 of the Action, the Examiner addresses Appellants' previous comments concerning SEQ ID NO:76 and whether or not this variant was associated with myelinopathies. The Examiner had previously stated that none of the mutations were specific for SEQ ID NO:76. However, Example 8 refers to identifying mutations in periaxin mRNA, of which SEQ ID NO:76 and SEQ ID NO:1 are variants of periaxin polynucleotide sequence (note Applicants' arguments above concerning the unrealistic restriction and unreasonable holding for non-consideration of these as species). Appellants assert that whether or not the alteration is identified in SEQ ID NO:76 or SEQ ID NO:1 is irrelevant, as these sequences and others listed in claim 3 were merely exemplary in nature.

On Page 20 of the Action, the Examiner considers Appellants' arguments that the specification provides the identification of exemplary mutations associated within the spectrum of myelinopathies and finds them unpersuasive, because the specification shows that different mutations are associated with a specific myelinopathy but allegedly provides no guidance as to

why such mutations are not associated or diagnostic of other types of myelinopathies. It is not a requirement for patentability to show *why* a particular alteration associates with myelinopathies, only *that* exemplary alterations associate with myelinopathies, and Appellants have provided not only multiple examples of such but described methods for others of skill in the art to identify additional examples.

On Page 21 of the Action, the Examiner states that there was consideration of Appellants' previous arguments that the specification has provided more than a sufficient number and content of working examples, including examples in the art. However, the Examiner considered these non-persuasive, because Appellants' arguments were allegedly directed to identification of embodiments that fall within the scope of the invention, as opposed to teaching which alterations were predictable associated with disease. That is, the Examiner alleges that Appellants' invite one to determine the embodiments that fall within the scope of the invention. Appellants consider this an inaccurate characterization of the specification, given that a number of periaxin alterations associated with the disease are taught in the specification, and given that it is not required to teach all of them. It is proper for Appellants to teach one of skill in the art how to identify other periaxin mutations in other myelinopathies and still remain enabled, which is a standard that the specification most definitely meets. This is not undue experimentation but absolutely routine in the art.

Furthermore, on Page 23 of the Action, the Examiner considers two different compound heterozygous mutations each associated with different myelinopathies, and states that the mere detection of a mutation does not allow a skilled artisan to predict which mutations are disease susceptible, disease-causing, or confer carrier status to an individual. Again, it is not required to provide predictable mutations but provide guidance how to determine if the mutations are diagnostic, which the enabled specification provides. As stated by Dr. Lupski, a skilled artisan would be able to distinguish between the two mutations, as clearly at least one group has already achieved using routine methods.

In summary, Appellants claims are enabled, given that a representative number of exemplary periaxin mutations were provided, a listing of exemplary myelinopathies was provided, and methods to determine others were taught in the specification. Further, it is not undue experimentation to perform the routine studies for identifying additional mutations, as other groups in the art published additional periaxin mutations for myelinopathies other then

DSN soon after the application was filed. Appellants respectfully request reversal of the Examiner's rejection.

C. Rejected Claims Under 35 U.S.C. §112, first paragraph, Enablement, are Separately Patentable

Claims 1-7, 35-40, and 42-61 are rejected under 35 U.S.C. §112, first paragraph, for enablement. Appellants respectfully disagree, as addressed above, and further notes that groups of the claims are separately patentable. The claims do not stand or fall together but are grouped as being separately patentable.

In particular, Appellant considers separate patentability for the grouping of the claims as follows: claims 1-7; claims 35-40 and 42; claims 43-48, claims 49-56; claims 57-60; and claim 67. All of the noted groups are separately patentable from each of the other groups because each grouping of claims concerns a different scope of the invention from the other groups, and the rejection of whether or not Appellant has provided sufficient disclosure to enable the claims is directly related to their scope. Appellant reiterates that each group of the claims is enabled.

VIII. CONCLUSION

Appellants have provided arguments that overcome the pending rejections. Appellants respectfully submit that the Action's conclusions that the claims should be rejected are unwarranted. It is therefore requested that the Board overturn the rejection of the Action.

Please date stamp and return the enclosed postcard to evidence receipt of this document.

Dated: June 13, 2005

Respectfully submitted,

By _____

Melissa L. Sistrunk
Registration No.: 45,579
FULBRIGHT & JAWORSKI L.L.P.
1301 McKinney, Suite 5100
Houston, Texas 77010-3095
(713) 651-3735
(713) 651-5246 (Fax)
Agent for Applicant

APPENDIX 1

PENDING CLAIMS

1. A method of diagnosing myelinopathy in an individual, said myelinopathy resulting from a periaxin alteration in the individual, comprising the steps of:

obtaining a sample containing nucleic acid from said individual;

assaying said sample for an alteration in a periaxin polynucleotide, wherein said assaying step provides said diagnosis.

2. The method of claim 1, wherein said periaxin polynucleotide is SEQ ID NO:76.

3. The method of claim 1, wherein said periaxin polynucleotide is SEQ ID NO:1, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, or SEQ ID NO:77.

4. The method of claim 1, wherein said myelinopathy is selected from the group consisting of Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSN), congenital hypomyelinating neuropathy (CHN), and Roussy-Levy syndrome (RLS).

5. The method of claim 1, wherein said assaying step further comprises a polymerase chain reaction.

6. The method of claim 5, wherein primers for said polymerase chain reaction are selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID

NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, and SEQ ID NO:26.

7. The method of claim 1, wherein said alteration is 3775G>A, 1216G>A, 4075-4077d, 1483G>C, 3394A>G, 3248C>G, 2763A>G, 2645C>T, 306C>T, 1491C>G, 2655T>C, 2145T>A, 1102C>T, 2289delT, 2787delC, 2857C>T, or 247ΔC.

35. A method of detecting the presence or absence of a mutation associated with a myelinopathy, said myelinopathy resulting from a periaxin mutation in the individual, the method comprising:

a) isolating a test nucleic acid from a subject, said test nucleic acid comprising a periaxin polynucleotide;

b) comparing the test nucleic acid to a reference wild-type periaxin polynucleotide; and

c) determining the differences between the test nucleic acid and the reference wild-type periaxin polynucleotide, wherein the differences are mutations in the periaxin polynucleotide of the subject, and wherein said detection of the presence or absence of the mutation is therein provided.

36. The method of claim 35, wherein said mutation is 2145T>A, 1102C>T, 2289delT, 2787delC, 2857C>T, or 247ΔC.

37. The method of claim 35, wherein said mutation encodes a defect of a periaxin polypeptide, wherein the defect is R953X, R368X, S929fsX957, R196X, V763fsX774, C715X, or R82fsX96.

38. The method of claim 35, wherein said periaxin polynucleotide is SEQ ID NO:1, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID

NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, or SEQ ID NO:77.

39. The method of claim 35, wherein said comparing step is by DHPLC, sequencing, hybridization, or a combination thereof.

40. The method of claim 35, wherein the myelinopathy is Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSN), congenital hypomyelinating neuropathy (CHN), or Roussy-Levy Syndrome (RLS).

42. The method of claim 35, wherein said mutation encodes a defect of a periaxin polypeptide, wherein the defect is E1259K, A406T, E1359delΔ, E495Q, R1132G, P1083R, I921M, A882V, T102T, P497P, or P885P.

43. A method of diagnosing myelinopathy in an individual comprising the steps of:

obtaining a sample containing nucleic acid from said individual;

assaying said sample for an alteration in a periaxin polynucleotide, wherein said alteration is associated with said myelinopathy, and wherein said myelinopathy comprises a prominent sensory neuropathy, wherein said assay provides said diagnosis.

44. The method of claim 43, wherein said periaxin polynucleotide is SEQ ID NO:76.

45. The method of claim 43, wherein said periaxin polynucleotide is SEQ ID NO:1, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID

NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, or SEQ ID NO:77.

46. The method of claim 43, wherein said assaying step further comprises a polymerase chain reaction.

47. The method of claim 46, wherein primers for said polymerase chain reaction are selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, and SEQ ID NO:26.

48. The method of claim 43, wherein said alteration is 3775G>A, 1216G>A, 4075-4077d, 1483G>C, 3394A>G, 3248C>G, 2763A>G, 2645C>T, 306C>T, 1491C>G, 2655T>C, 2145T>A, 1102C>T, 2289delT, 2787delC, 2857C>T, or 247ΔC.

49. A method of detecting a polymorphism or mutation in a periaxin polynucleotide of an individual, comprising the steps of:

obtaining a sample comprising said periaxin polynucleotide from said individual;

assaying said periaxin polynucleotide for the polymorphism or mutation.

50. The method of claim 49, wherein said periaxin polynucleotide comprises SEQ ID NO:76.

51. The method of claim 1, wherein said myelinopathy is Dejerine-Sottas syndrome.

52. The method of claim 1, wherein said individual is suspected of having the myelinopathy.

53. The method of claim 1, wherein the alteration comprises a homozygous periaxin mutation.

54. The method of claim 1, wherein the alteration comprises a compound heterozygous periaxin mutation.

55. The method of claim 43, wherein the alteration comprises a homozygous periaxin mutation.

56. The method of claim 43, wherein the alteration comprises a compound heterozygous periaxin mutation.

57. A method of identifying an individual suspected of having myelinopathy or being a carrier of myelinopathy, comprising the steps of:

obtaining from said individual a sample comprising nucleic acid; and

assaying said sample for an alteration in a periaxin polynucleotide, wherein the presence of the alteration identifies said individual as having periaxin-associated myelinopathy or being a carrier of periaxin-associated myelinopathy.

58. The method of claim 57, wherein said myelinopathy comprises a prominent sensory neuropathy.

59. The method of claim 57, wherein the alteration comprises a homozygous periaxin mutation.

60. The method of claim 57, wherein the alteration comprises a compound heterozygous periaxin mutation.

61. A method of identifying an individual suspected of having myelinopathy or being a carrier of myelinopathy, comprising the steps of:

obtaining from said individual a sample comprising genomic DNA having two PRX alleles; and

assaying said sample for an alteration in a periaxin polynucleotide, wherein the presence of the alteration in the periaxin polynucleotide is indicative of an alteration in at least one of the PRX alleles, wherein the presence of the alteration in both PRX alleles identifies said individual as having periaxin-associated myelinopathy and wherein the presence of the alteration in one allele identifies said individual as being a carrier of periaxin-associated myelinopathy.